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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/690,199	10/21/2003	Igor Astsaturov	API-02-13-US	3672
7590 Patrick J. Halloran Aventis Pasteur Knerr Building Discovery Drive Swiftwater, PA 18370			EXAMINER SHEN, WU-CHENG WINSTON	
			ART UNIT 1632	PAPER NUMBER
			MAIL DATE 01/07/2008	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/690,199	<b>Applicant(s)</b> ASTSATUROV ET AL.	
	<b>Examiner</b> Wu-Cheng Winston Shen	<b>Art Unit</b> 1632	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 31 October 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1 and 4-22 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1 and 4-22 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 21 October 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### DETAILED ACTION

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 31, 2007 has been entered.

Claims 1 and 4 have been amended. Claims 2 and 3 have been canceled. Claims 1 and 4-22 are pending, and currently under examination.

This application 10/690,199 filed on Oct. 21, 2003 claims benefit of provisional application 60/420,425 filed on Oct. 22, 2002. The publication number of this application 10/690,199 is US 2004/0223949 A1, published on Nov. 11, 2004.

Applicant is referred to 37 CFR 1.121 for how to make amendments to the claims. 37 CFR 1.121 (c)(4) states that the context of cancelled claims should not be presented. However, because claims 2 and 3 have the status identifier "Cancelled" and the Remarks indicate claim 3 as cancelled, claims 2 and 3 are considered as cancelled. The Examiner called the attorney of the record Patrick J. Halloran on 12/31/2007 and the attorney verified that claim 2 has been cancelled. Applicant is requested to comply with 37 CFR 1.21 in any future reply.

### *Claim Objections*

2. Previous objection of claims 1, 5, 6, 11, and 12 for recitation of non-elected inventions as Applicant elected nucleic acid encoding a tumor antigen (for claim 1), but claim 1 encompasses protein therapy, a non-elected subject matter, is **withdrawn** because claim 1 has been amended.

***Claim Rejection – 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

3. Claims 8-10 and 14-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. *This rejection is necessitated by claim amendments by Applicant filed on 10/31/2007.*

Claims 8-10 and 14-17 recite the following limitations: (i) "the cytokine" (claims 8-10), (ii) "the cytokine is a T cell activating cytokine" (claim 14), and (iii) "the T cell activating cytokine" (claims 15-17). There is insufficient antecedent basis for these limitations in the claims. Claims 8-10 and 14-17 depend from claim 1. Claim 1 has been amended and no longer recites a cytokine.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

***New Matter Rejection***

4. Claims 1, and 4-22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection. 37 CFR 1.118 (a) states that "No amendment shall introduce **new matter** into the disclosure of an application after the filing date of the application".

Claim 1 is directed to a method for treating melanoma comprising: a) administering to a host a composition containing a nucleic acid encoding a tumor antigen such that the host develops an immune response against the tumor antigen; and, b) subsequently administering *a therapeutically effective amount of interferon* to the host; whereby the combination of steps a) and b) provides an enhanced T cell response in the host relative to that which occurs following step a) alone. Claims 4-22 depend from claim 1.

In the response filed on 10/31/2007, Applicant asserted that as shown in Applicants' Examples 1 and 2 (see, in particular, paragraph [0083]), therapeutically effective amounts of IFN- $\alpha$ 2b were found to range from the initial 20 megaunits (MU) down to approximately six megaunits depending upon the toxicity observed in each patient. As shown in the application, this may vary slightly depending on the particular patient being treated or interferon being utilized but selection of the effective dose is within the purview of the ordinary skilled artisan. The Examiner found Applicant's assertion not persuasive.

It is noted that there are different types of interferons and the specification only discloses the therapeutic use of IFN- $\alpha$ 2b in the claimed method of treating melanoma. In the case IFN- $\alpha$ 2b, Example 2 of the specification also alerts a skilled artisan the following: Dose reductions and treatment delays due to toxicity were experienced by all 7 patients (Table 2) which is somewhat higher than the 33% incidence reported for 396 patients in the E1694

Intergroup trial (Kirkwood, 2002, *supra*). Therefore, in the absence of proper written description of the phrase "a therapeutically effective amount of interferon", the specification provides no reason to assert that a given interferon used for a given regimen of treatment only vary slightly depending on the particular patient being treated or interferon being utilized and that the selection of the effective dose is within the purview of the ordinary skilled artisan. It is worth noting that more than three- fold differences in dose of IFN- $\alpha$ 2b considered to be therapeutically effective, i.e. range from the initial 20 megaunits (MU) down to approximately six megaunits, is not considered as "vary slightly" as Applicant argues. The concern of lack of proper written description of the phrase "a therapeutically effective amount of interferon" is further compounded by the therapeutic efficacy of interferon alone, in the absence of administration of nucleic acid encoding a tumor antigen as claimed in instant application. In this regard, **Shah et al.** reviewed adjuvant therapy of melanoma and states the following: There have been no meaningful trials addressing adjuvant chemotherapy in melanoma because all trials have been underpowered. Adjuvant interferon- $\alpha$  has been tested both at high dose and at lower doses. None of the trials have shown a reproducible benefit in survival, although the high-dose trials and some of the low-dose trials have shown improvement in time to relapse. These experiences raise the question of whether chronic administration is more important than dose. An adjuvant pegylated interferon- $\alpha$  trial using a 5-year treatment period is currently under investigation. At least 7 randomized adjuvant vaccine trials have been published, but none have shown a beneficial effect on relapse-free or overall survival except in subset analyses (See Results, left column, page 217, **Shah et al.**, Adjuvant therapy of melanoma, *Cancer J.* 13(3):217-22, 2007). The Examiner acknowledges the trials reviewed by Shah et al. are not identical regimen

compared to the claimed invention, which includes administration of a nucleic acid encoding a tumor antigen first before administration of interferon. Nevertheless, the efficacy, as revealed by therapeutically effective amount, of interferon therapy by itself is certainly a critical factor to be considered when a given interferon is administered after of a nucleic acid encoding a tumor antigen. The specification is silent with regard to written description of how a therapeutically effective amount of a given interferon should be determined in the claimed method.

Furthermore, the disclosed doses of IFN- $\alpha$ 2b in Example 2 appear to be problematic in the claimed method of treatment of melanoma because more than 1/3 of the patients tested exhibited an unintended toxic effect, rather than a therapeutic effect.

Applicants are reminded that it is their burden to show where the specification supports any amendments to the claims. See 37 CFR 1.121 (b)(2)(iii), the MPEP 714.02, 3<sup>rd</sup> paragraph, last sentence and also the MPEP 2163.07, last sentence.

MPEP 2163.06 notes, "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire

application is often necessary to determine whether or not “new matter” is involved. Applicant should therefore specifically point out the support for any amendments made to the disclosure.

5. Previous scope of enablement rejection of claims 1, and 4-22 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating melanoma in a host by administration to a host a polynucleotide encoding a melanoma-associated antigen, which comprises antigenic determinants that induce immune response, followed by multiple administration of interferon- $\alpha$ 2b at 20 MU/m<sup>2</sup>/day, 5 days/week for 4 weeks, wherein said administering of the polynucleotide and subsequent administration of interferon- $\alpha$ 2b result in an increased T cell response in the host relative to the T cell response that occurs following administering of the polynucleotide alone, **does not** reasonably provide enablement for treating melanoma by administration of 1) any tumor antigen other than a melanoma-associated antigen, or 2) subsequent administration of any interferon other than interferon- $\alpha$ , or 3) administration of interferon- $\alpha$ 2b at any dose for any regimen, is ***maintained*** for the reasons of record advanced on pages 4-9 of the Non-Final office action mailed on 07/25/06, and elaborated on pages 3-8 of the Final office action mailed on 05/01/2007. The rejection of claim 3 is moot because claim 1 has been canceled.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to perform the invention commensurate in scope with these claims.

It is noted that based on the claim amendments filed by Applicant on 10/31/2007, and upon further consideration, the enabled scope has been modified in the following aspects.



Different routes of administration of a nucleic acid encoding a melanoma-associated antigen as a vaccine for generation of cytotoxic T lymphocyte (CTL) immune response are considered as enabled because various routes of administration other than intratumoral administration are supported by in the literature at the time of filing of instant application.

First, a polynucleotide encoding a tumor antigen other than a melanoma-associated antigen is considered as *not* enabled because not all tumor antigens are expressed in melanoma cells and the expression of a melanoma-associated antigen on melanoma cells is required for the induced cytotoxic T lymphocyte (CTL) mediated cell lysis specifically targeting to melanoma cells. Second, subsequent administration of any interferon other than interferon- $\alpha$ 2b is *not* enabled because the specification only discloses administration of interferon- $\alpha$ 2b and the status of art at the time of filing indicated the unpredictabilities in the efficacy of adjuvant interferon therapy of melanoma. For instance, Poole et al. reported that upon interferon- $\gamma$  treatment, reduced melanosomal antigen expression and recognition of melanoma cells by cytotoxic T cells were observed (See **Poole et al.**, Interferon-gamma reduces melanosomal antigen expression and recognition of melanoma cells by cytotoxic T cells. *Am J Pathol.* 160(2):521-8, 2002). Third, the status of art indicated the unpredictabilities regarding the dose and the regimen of administration of interferon- $\alpha$ 2b in the treatment of melanoma.

On the other hand, upon further consideration, the Examiner notes that different routes of administration of a nucleic acid encoding a melanoma-associated antigen as a vaccine for generation of cytotoxic T lymphocyte (CTL) immune response are considered as enabled because various routes of administration other than intratumoral administration are supported by the literature. For examples, **Yamanaka et al.** disclose intramuscular injection of Sindbis DNA

encoding Gp100 and IL-18 (See title and abstract, Yamanaka et al. Induction of antigen-specific immune responses against malignant brain tumors by intramuscular injection of sindbis DNA encoding gp100 and IL-18. *DNA Cell Biol.* 24(5):317-24, 2005), and **Leitner et al.** discloses both intramuscular and intravenous injection of Fowlpox virus of DNA vaccine (See Figure 3, Leitner et al. Type I Interferons are essential for the efficacy of replicase-based DNA vaccines, *Vaccine*, 24(24):5110-8, 2006).

***Applicant's Arguments and Examiner's response to applicant's Arguments***

(1) *Applicant's arguments/claim amendments:* In the claim amendments filed on 10/31/2007, claim 1 no longer recites a composition containing a tumor antigen and fragment, and claim 1 now recites "A method for treating melanoma comprising: a) administering to a host a composition containing a nucleic acid encoding a tumor antigen ---". It is noted that in the Remarks filed on 10/31/2007, Applicant did not elaborate or argue the breadth of amended claims regarding whether administration of a DNA vaccine containing a nucleic acid encoding any tumor antigen can be used for treating melanoma.

*In response:* The Examiner notes that a polynucleotide encoding *any tumor antigen* other than a melanoma-associated antigen is considered as *not* enabled for the claimed method for treating melanoma. This aspect of rejection is necessitated by the claimed amendments filed on 10/31/2007 limiting to a method of treating melanoma, instead of a method of treating cancer. It is noted that not all tumor antigens are expressed in melanoma cells and the expression of a melanoma-associated antigen on melanoma cells is required for the induced cytotoxic T

lymphocyte (CTL) mediated cell lysis specifically targeting to melanoma cells. For instance, in the art, **Vujanovic et al.** have reviewed tumor antigens and stated that there are four categories of tumor associated antigens (TAA): The first category is cancer-testis antigens. These are proteins encoded by genes expressed in various tumors but not in normal tissues, except for testis and placenta. Antigens that belong to this group are MAGE, GAGE, and BAGE families, as well as NY-ESO-1 and its alternative ORF products LAGE and CAMEL. The second group represents differentiation antigens that are shared between tumors and the normal tissue from which the tumor arose. *Most identified to date are expressed in melanoma and normal melanocytes, such as tyrosinase, Melan-A/MART-1, gp100* (which is the elected species of tumor associated antigens for prosecution of instant application), *TRP-1, and TRP-2*. The third category is tumor-specific antigens. These antigens are generated by point mutations (e.g., p53, Ras, CDK4,  $\beta$ -catenin) or tumor-specific splicing aberrations in genes that are ubiquitously expressed [e.g., TRP-2/INT2], and are expressed only in tumors from the patient from whom they were identified (unlike cancer-testis antigens). These molecular changes are associated with neoplastic transformation and/or progression. The fourth group of antigens is widely occurring, over-expressed TAA. These are proteins that have been detected in histologically different types of tumors (often with no preferential expression on a certain type of cancer) as well as in many normal tissues, generally with lower expression levels. Some of the antigens belonging to this group include survivin, MUC1/2,  $\alpha$ -fetoprotein (AFP) and EphA2, among others (See Table I, page 302, Vujanovic et al., Melanoma cancer vaccines and anti-tumor T cell responses. *J Cell Biochem.* 102(2):301-10, 2007).

Relevant to the specificities of different tumor associated antigen, it is worth noting that not all antigenic determinants of a given melanoma associated antigen can elicit T cell mediated immune response. In this regard, for instance, **Valmori et al.**, reported that a CD8+ T cell response to the peptide analog Melan-A(26-35 A27L) was detectable *ex vivo* at a later time point, whereas CD8+ T cells specific for peptide tyrosinase(368-376) were detected only after *in vitro* peptide stimulation, and *no detectable CD8+ T cell response to peptide gp100(457-466) was observed* (See abstract, Valmori et al., Simultaneous CD8+ T cell responses to multiple tumor antigen epitopes in a multi-peptide melanoma vaccine. *Cancer Immun.* 3:15, 2003).

(2) *Applicant's arguments/claim amendments*: In the claim amendments filed on 10/31/2007, claim 1 no longer recites subsequently administering to the host a high dose of cytokine , and claim 1 now recites "A method for treating melanoma comprising: a) administering to a host a composition containing a nucleic acid encoding a tumor antigen such that the host develops an immune response against the tumor antigen; and b) subsequently administering a therapeutically effective amount of interferon to the host". It is noted that in the Remarks filed on 10/31/2007, Applicant did not elaborate or argue the breadth of amended claims regarding whether subsequently administration of any interferon can be used for the claimed method for treating melanoma.

With respect to the aspect of the rejection regarding the dose and timing of cytokine (or interferon as amended on 10/31/2007) to be administered, Applicant does argue that claim 1 has been amended to require administration of a "therapeutically effective amount of interferon". Applicant argues that as shown in Applicants' Examples 1 and 2 (see, in particular, paragraph

[0083]), therapeutically effective amounts of IFN- $\alpha$ 2b were found to range from the initial 20 megaunits (MU) down to approximately six megaunits depending upon the toxicity observed in each patient. As shown in the application, this may vary slightly depending on the particular patient being treated or interferon being utilized but selection of the effective dose is within the purview of the ordinary skilled artisan. Applicant further argues that clinical regression was observed in patients treated with IFN- $\alpha$ 2b 1.5 and 6 months subsequent to the last administration of antigen and the others showed no disease progression. Applicant indicated that the term "subsequently" directs the skilled artisan to that period of time during which administration of an interferon would be effective, and the exact timing of the "subsequently administered" dose may vary between patients but selection of the effective time is within the purview of the ordinary skilled artisan.

*In response:* The Examiner notes that subsequently administration of *any interferon* to be used for the claimed method for treating melanoma is considered as *not* enabled. This aspect of rejection is necessitated by the claimed amendments filed on 10/31/2007 limiting to a method of treating melanoma, instead of a method of treating cancer. It is noted that the specification disclosed the following in one embodiment, IFN- $\alpha$ 2b (Schering Canada, Pointe-Claire, Quebec) may be administered using the dosages set forth by Kirkwood, et al. (*J.Clin.Oncol.* 14: 7-17, 1996; 20 MU/m<sup>2</sup>/d IV days/week.times.4 weeks), and dosages may be discontinued and restarted as necessary (See paragraph [0072], US 2004/0223949, the publication of instant application). Consistently, Applicant's own publication disclosed the same regimen (See abstract, **Astsaturrov et al.**, Amplification of virus-induced anti-melanoma T-cell reactivity by high-dose interferon-alpha2b: implications for cancer vaccines.

*Clin Cancer Res.* 9(12):4347-55, 2003). However, in the art at the time of filing, the administration of IFN- $\alpha$ 2b for treatment of melanoma was and has been unpredictable. For instance, **Sabel et al.** stated the following: The Eastern Cooperative Oncology Group trial EST 1684, showed that a high-dose regimen involving an induction phase of intravenous interferon-alpha-2b 20 MU/m<sup>2</sup> 5 days a week for 4 weeks, followed by a maintenance phase of subcutaneous 10 MU/m<sup>2</sup> 3 days a week for the remainder of a year, led to significant improvements in both disease-free and overall survival compared with observation. On the basis of these results, the US FDA approved high-dose interferon-alpha-2b for the post-surgical adjuvant therapy of high-risk melanoma. *Unfortunately, the results of subsequent trials involving high-dose interferon-alpha-2b have not been as clear and its role in the adjuvant treatment of melanoma remains controversial. Concerns remain regarding the design and interpretation of the clinical trials, the cost and toxicity of treatment, and the appropriate selection of patients who should be treated* (See, Sabel et al., abstract, Is there a role for adjuvant high-dose interferon- $\alpha$ 2b in the management of melanoma? *Drugs*, 63(11):1053-8, 2003). In light of the unpredictabilities regarding the interferon- $\alpha$ 2b dose regimen for treating melanoma, only the dose regimen disclosed in the specification of instant application is considered enabled.

(3) *Applicant's arguments:* With respect to the aspect of the rejection regarding the breadth of the claims relating to treatment by administration of a polynucleotide and/or a cytokine via any route, Applicant has argued on the record that the claimed invention is not dependent upon a particular route of administration (i.e., direct administration to a particular site) (See pages 3-5 of Applicant's response filed on 01/25/2007). Applicant argues that it is the

combination of the administration of a nucleic acid encoding a tumor antigen and the subsequent administration of a high dose of cytokine that is inventive. All that is required in part (a) of claim 1 is that a nucleic acid encoding a tumor antigen is administered such that the host develops an immune response to the tumor antigen. As stated in the specification, many suitable routes of administration are in fact available to one of skill in the art. Even if it were true that a particular route of administration suitable for one type of cancer was not suitable to every other type of cancer, it would not be an undue burden for the skilled artisan to select another route suitable to that other type of cancer. As suggested in Applicants' specification and the articles cited by the Examiner, many such routes are known in the art. In this regard, Applicant further argues, in addition, the successful administration of tumor antigens to human beings by several different routes (i.e., intradermal, subcutaneous, intranodal, and intravenous) has been shown by, for example, Marshall, et al. (J. Clin. Oncol. 18(23): 3964-3973 (2000), van der Burg, et al. (Clin. Cancer Res., 8:1019-1027 (2002), Astatsturov, et al. (by the Applicants; Clin. Cancer Res. 9:4347-4355 (2003), Karakinas, et al. (J. Immunol. 171: 4898-4904 (2003), van Baren, et al. (J. Clin. Oncol. 23 (35): 9008-9021 (2005). Thus, the skilled artisan would have many routes to choose from in practicing the claimed invention.

*In response:* Upon further consideration, in light of Applicant's previous arguments filed on 01/25/2007 and claim amendments filed on 10/31/2007, the scope of enablement rejection regarding the aspect of the rejection limited to the direct administration of nucleic acid encoding a melanoma associated antigen is *withdrawn* as indicated in the beginning of the revised scope of enablement rejection in this office action.

***Claim Rejection – 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Previous rejection of claims 1, 3-8, 14-15 under 35 U.S.C. 102(b) as being anticipated by Paoletti, 1999 (U.S. patent number 5,942,235; issued on August 24, 1999), is ***withdrawn*** because Applicant's arguments in combination with claim amendments were found persuasive.

Paoletti, 1999 does not teach explicitly the limitation "subsequently administering a therapeutically effective amount of interferon to the host" and the limitation "whereby the combination of steps a) and b) provides an enhanced T cell response in the host relative to that which occurs following step a) alone", as recited in claim 1 of instant application.

***Conclusion***

7. No claim is allowed.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).



Application/Control Number:  
10/690,199  
Art Unit: 1632

Page 16

Any inquiry concerning this communication from the examiner should be directed to Wu-Cheng Winston Shen whose telephone number is (571) 272-3157 and Fax number is 571-273-3157. The examiner can normally be reached on Monday through Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the supervisory patent examiner, Peter Paras, can be reached on (571) 272-4517. The fax number for TC 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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